scope of the invention. A substitute specification is being prepared and will be submitted under separate cover to correct obvious typographical and grammatical errors, as well as to incorporate the newly added claims 3-64. No new matter is added as a result of the additional claims.

Claim 1 has been amended to correct obvious typographical and grammatical errors, and has not been narrowed.

The specification is amended to include a reference to the priority application, United States Provisional Patent Application No. 60/284,005, filed April 16, 2001.

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

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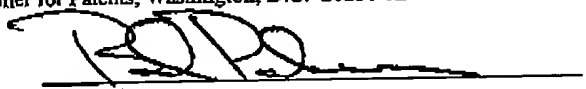

April 16, 2002
Date

Brad Pedersen

Application No. 09/855,027

ATTACHMENT
REDLINED AMENDMENT

In the Specification

Page 1, line 4:

RELATED APPLICATIONS

This application claims priority to United States provisional patent Application No. 60/284,005, filed April 16, 2001, which is hereby incorporated by reference herein.

In the Claims

Please cancel claim 2 without prejudice or disclaimer.

Please substitute the following amended claims for those currently pending:

1. (Once Amended) A method of transplanting a donor tissue, the method comprising the steps of:

administering a bone marrow cell transplant from a donor to a recipient;

administering a conditioning treatment to the recipient that avoids neutropenia;

administering an immune blockade treatment to the recipient[,]; and

transplanting a donor tissue from the donor to the recipient[,];

wherein the donor is a clinical cadaver and the tissue transplant, conditioning treatment, and bone marrow cell transplant are completed within a single continuous forty-eight hour period of time.

2. (Canceled) The inventions as described herein.

Please add new claims 3-64:

--3. A method of transplanting a donor tissue from a donor to a recipient, the method comprising:

creating a mixed chimeric immune system in the recipient that is a chimer of the donor and recipient immune systems; and

transplanting the donor tissue from the donor to the recipient;

with the creation a mixed chimeric immune system including:

infusing donor cells from the donor into the recipient that cause the production of immune system cells in the recipient that have at least one cellular marker that is characteristic of the donor immune system;

administering a conditioning treatment to the recipient that avoids neutropenia; and

administering an immune blockade treatment to the recipient.

4. The method of claim 3, wherein the donor is a clinical cadaver and the donor tissue transplant, conditioning treatment, and the infusion of the donor cells are completed within a single continuous forty-eight hour period of time.

5. The method of claim 3, wherein the conditioning treatment is accomplished such that an amount of granulocytes in the recipient's blood decreases by less than 30%.

6. The method of claim 3, wherein the donor cell infusion is performed after the step of transplanting the donor tissue.

7. The method of claim 3, further comprising pretreating the recipient with pretreatment cells from the donor prior to the infusion of the donor cells.

8. The method of claim 3, wherein the conditioning treatment is accomplished by administering at least one drug chosen from the group consisting of fludarabine phosphate, busulfan, and cyclophosphamide.

9. The method of claim 3, wherein administering the conditioning treatment is accomplished by administering at least one drug chosen from the group consisting of a purine

nucleoside analog, deoxycoformycin, 2-chloro-2' deoxyadenosine, ifosamide, etoposide, mitoxantrone, doxorubicin, cisplatin, carboplatin, cytarabine, paclitaxel, nitrosoureas, melphalan, thiotepa, antilymphocyte serum, anti-thymocyte globulin, and anti-lymphocyte globulin.

10. The method of claim 3, wherein administering the immune blockade treatment is accomplished by administering at least one of the compounds selected from the group consisting of anti-CD40L, sirolimus, CTLA4Ig, LEA29Y, and compounds that inhibit the binding of B7 to CD28.

11. The method of claim 3, wherein the conditioning treatment is started less than six days prior to the infusion of the donor cells.

12. The method of claim 3, wherein the conditioning treatment is started less than two days prior to the infusion of the donor cells.

13. The method of claim 3, wherein the donor tissue includes pancreatic islet cells and infusing the donor cells and transplanting the donor tissue are accomplished within a 96 hour time period.

14. The method of claim 3, wherein the donor cell infusion is performed by administering bone marrow from the donor to the recipient.

15. The method of claim 3, wherein the donor cell infusion is performed by administering stem cells to the recipient.

16. The method of claim 15, wherein the donor cell infusion includes administering stem cells to the recipient on more than one day.

17. The method of claim 3, wherein the donor cell infusion includes administering stem cells collected from the peripheral blood of the donor.

18. The method of claim 3, wherein the conditioning treatment includes low-dose irradiation of less than 500 GY.

19. The method of claim 18, wherein the conditioning treatment includes low-dose total body irradiation of less than 300 GY.

20. A kit for treating a patient receiving an infusion of stem cells from a donor, the kit comprising:

at least one dosage of at least one conditioning treatment drug;

at least one dosage of at least one immune blockade drug; and

information for delivering the drugs in a sequence and at predetermined levels such that mixed chimerism is induced in the patient in less than six days.

21. The kit of claim 20, wherein the at least one conditioning treatment drug is chosen from the group consisting of a purine nucleoside analog, deoxycoformycin, 2-chloro-2' deoxyadenosine, ifosamide, etoposide, mitoxantrone, doxorubicin, cisplatin, carboplatin, cytarabine, paclitaxel, nitrosoureas, melphalan, thiotepa, antilymphocyte serum, anti-thymocyte globulin, and anti-lymphocyte globulin.

22. The kit of claim 20, wherein the at least one immune blockade drug is chosen from the group consisting of anti-CD40L, CTLA4Ig, sirolimus, and compounds that inhibit the binding of B7 to CD28.

23. The kit of claim 20, wherein the information includes instructions for a pretreatment step of administering cells from the donor to the recipient prior to the stem cell infusion.

24. The kit of claim 20, wherein the information describes administration of drugs and drug dosages for reducing the number of granulocytes in the recipient by no more than 30%.

25. The kit of claim 20, wherein the instructions set forth delivering the drugs in a sequence and at predetermined levels such that mixed chimerism is induced in the patient in less than seven days.

26. The method of claim 25, wherein the information sets forth starting the at least one conditioning treatment drug less than seven days prior to the stem cell infusion.

27. A method of treating a patient with materials from a donor, the method comprising:

transplanting infusing donor cells from the donor into the recipient that cause the production of immune system cells in the recipient that have at least one cellular marker that is characteristic of the donor immune system; and

creating a mixed chimeric immune system in the patient that is a chimer of the immune systems of the donor and the patient, including:

administering a conditioning treatment to the patient in a period of less than six days prior to transplanting the bone marrow cells that avoids neutropenia in the patient; and

administering an immune blockade treatment to the patient that causes lymphocyte specific immune suppression;

such that the mixed chimeric immune system is at least 5% donor-specific as measurable in peripheral blood of the patient.

28. The method of claim 27, wherein administering the conditioning treatment is started less than six days prior to transplanting the donor cells.

29. The method of claim 27, wherein administering the conditioning treatment is started less than two days prior to transplanting the donor cells.

30. The method of claim 27, wherein administering the conditioning treatment is performed with at least one drug selected from the group consisting of fludarabine phosphate, busulfan, and cyclophosphamide.

31. The method of claim 27, wherein administering the immune blockade treatment is performed with at least one treatment selected from the group consisting of rapamycin, co-stimulatory blockade, CTLA4Ig, LEA29Y, and anti-lymphocyte serum (ALS).

32. The method of claim 27, further comprising a pretreatment step of administering pretreatment cells from the donor to the recipient prior to transplanting the donor cells.

33. The method of claim 27, wherein the donor cells are stem cells taken from the donor's blood.

34. The method of claim 27, wherein transplanting the donor cells is accomplished by administering donor stem cells to the recipient.

35. The method of claim 27, wherein the donor cell transplant is performed by administering bone marrow to the recipient.

36. The method of claim 27, wherein the donor cell transplant is performed by administering stem cells to the recipient.

37. A method of treating a patient with tissue taken from a donor, the method comprising:

removing the tissue from the donor, the tissue comprising immune system cells other than spleen cells; and

inducing a condition of mixed chimerism in the patient according to a method of:

preparing the recipient with a conditioning treatment that reduces the number of the neutrophil cells or macrophage cells in blood of the recipient such that neutropenia is avoided;

transplanting the tissue from the donor into the recipient; and

administering an immune blockade;

such that the tissue contributes the function of the recipient's immune system.

38. The method of claim 37, wherein the conditioning treatment and the transplanting of the tissue occurs within a continuous 48 hour period.

39. The method of claim 37, wherein the administering of the immune blockade treatment is accomplished by administering at least one of the compounds selected from the group consisting of anti-CD40L,CTLA4Ig, LEA29Y, sirolimus, and compounds that inhibit the binding of B7 to CD28.

40. A method of transplanting pancreatic islet cells from a donor to a recipient, the method comprising:

administering a pancreatic islet cell transplant from the donor to the recipient; and

inducing a state of mixed chimerism in the recipient according to a method that includes:

infusing donor cells within 96 hours of the pancreatic islet cell transplant from the donor into the recipient, the donor cells causing the production of immune system cells in the recipient that have at least one cellular marker that is characteristic of the donor immune system;

administering a conditioning treatment to the recipient that is mildly myeloablative; and

administering an immune blockade treatment to the recipient.

41. The method of claim 40, wherein the donor cell infusion and the pancreatic islet cell transplant both occur within a twelve hour time period.

42. The method of claim 40, wherein the state of mixed chimerism is such that a donor chimerism level in the recipient of at least 15% is achieved as determined by measurements taken from the recipient's peripheral blood samples.

43. The method of claim 40, further comprising administering a cell pretreatment from the donor to the recipient prior to the infusion of the donor cells.

44. The method of claim 43, further comprising administering an antilymphocyte serum within 48 hours after an end of the cell pretreatment.

45. A medically modified non-human animal, incorporating cells from a donor by a process comprising:

administering donor cells from the donor into the non-human animal that cause the production of immune system cells in the non-human animal that cause the production of immune system cells in the non-human animal that have at least one cellular marker that is characteristic of the donor immune system;

administering a mildly myeloablative conditioning treatment to the animal in a period of less than six days;

administering an immune blockade treatment to the animal; and

wherein the animal has a mixed chimeric immune system having at least 1% donor-specific mixed chimerism.

46. The animal of claim 45, wherein the mildly myeloablative conditioning treatment comprises fludarabine or cyclophosphamide.

47. The animal of claim 45, wherein the animal is a mouse, rat, pig, sheep, or a monkey.

48. A method of treating a cancerous condition in a patient with materials from a donor, the method comprising:

inducing a graft versus tumor effect in the patient for treating the cancerous condition by transplanting cells from the donor to the patient;

inducing a state of mixed chimerism in the patient by a method that includes:

administering donor cells from the donor into the patient that cause the production of immune system cells in the patient that cause the production of

immune system cells in the recipient that have at least one cellular marker that is characteristic of the donor immune system;

administering a conditioning treatment to the patient, such that neutropenia is avoided;

administering an immune blockade treatment to the patient that causes lymphocyte-specific immune suppression; and

such that at least 1% donor-specific chimerism is achieved, as measurable in peripheral blood of the patient.

49. The method of claim 48, wherein the transplanted cells are the donor cells.

50. The method of claim 48, wherein the conditioning treatment results in an amount of granulocytes in the patient's blood decreasing by less than 30% during the conditioning treatment.

51. The method of claim 48, wherein the conditioning treatment includes administering at least one drug chosen from the group consisting of fludarabine phosphate, busulfan, and cyclophosphamide.

52. The method of claim 48, wherein the conditioning treatment includes administering at least one drug chosen from the group consisting of a purine nucleoside analog, deoxycoformycin, 2-chloro-2' deoxyadenosine, ifosamide, etoposide, mitoxantrone, doxorubicin, cisplatin, carboplatin, cytarabine, paclitaxel, nitrosoureas, melphalan, thiotepa, antilymphocyte serum, anti-thymocyte globulin, and anti-lymphocyte globulin.

53. The method of claim 48, wherein the immune blockade treatment includes administering at least one of the compounds selected from the group consisting of anti-CD40L, CTLA4Ig, LEA29Y, sirolimus, and compounds that inhibit the binding of B7 to CD28.

54. The method of claim 48, wherein the conditioning treatment is performed less than six days prior to transplanting the donor cells.

55. The method of claim 48, wherein the conditioning treatment is performed within two days prior to transplanting the donor cells.

56. A method of treating an immune system disorder in an immune system of a patient, the method comprising:

infusing donor cells from the donor into the patient that cause the production of immune system cells in the patient that cause the production of immune system cells in the recipient that have at least one cellular marker that is characteristic of the donor immune system;

creating a state of at least 1% donor-specific mixed chimerism in the patient's immune system as measurable in peripheral blood of the patient in order to treat the immune system with a method that includes:

administering a conditioning treatment to the patient that avoids neutropenia; and

administering an immune blockade treatment to the patient that causes lymphocyte-specific immune suppression.

57. The method of claim 56, wherein the immune system disorder is diabetes.

58. The method of claim 57, wherein the method is performed before the diabetes has caused abnormal insulin levels in the patient.

59. The method of claim 56, wherein an amount of granulocytes in the patient's blood decreases by less than 30% during the conditioning treatment.

60. The method of claim 56, further comprising pretreating the patient with pretreatment cells from the donor before the infusion of the donor cells.

61. The method of claim 56, wherein the conditioning treatment includes administering at least one drug chosen from the group consisting of fludarabine phosphate, busulfan, and cyclophosphamide.

62. The method of claim 56, wherein the conditioning treatment includes administering at least one drug chosen from the group consisting of a purine nucleoside analog, deoxycoformycin, 2-chloro-2' deoxyadenosine, ifosamide, etoposide, mitoxantrone, doxorubicin, cisplatin, carboplatin, cytarabine, paclitaxel, nitrosoureas, melphalan, thiotepa, antilymphocyte serum, anti-thymocyte globulin, and anti-lymphocyte globulin.

63. The method of claim 56, wherein the immune blockade treatment includes administering at least one of the compounds selected from the group consisting of anti-CD40L, CTLA4Ig, LEA29Y, sirolimus, and compounds that inhibit the binding of B7 to CD28.

A3 Cont.

64. The method of claim 56, wherein the conditioning treatment is performed within less than six daysprior to the donor cell infusion.--

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Application No.:	09/855,027
File No.:	1432.05US02
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